OPTN/UNOS Liver and Intestinal Organ Transplantation Committee
Report to the Board of Directors
November 12-13, 2014
St. Louis, Missouri

David Mulligan, MD, FACS, Chair
Ryutaro Hirose, MD, Vice Chair

Contents

Action Items **2**
1. Proposal to Cap the HCC Exception Score at 34 2
2. Proposal to Delay the HCC Exception Score Assignment 2

Committee Projects **3**
3. Liver Distribution Redesign Modeling (Redistricting of Regions) 3
4. National Review Board for MELD/PELD Exceptions 4
5. Develop materials to Educate RRB Members and Promote Consistent 4
6. Proposed Membership and Personnel Requirements for Intestine Transplant Programs 5
7. Ongoing Review of MELD/PELD Exceptions 6

Committee Projects Pending Implementation **6**
8. Adding Serum Sodium to the MELD Score 6
9. Re-instate the No Appeal, No Withdrawal Button for Denied MELD/PELD Exceptions 7

Implemented Committee Projects **7**
10. Proposal for Regional Distribution of Livers for Critically Ill Candidates, (Share 35) 7

Review of Public Comment Proposals **8**
11. Proposal to Modify Existing or Establishing New Requirements for the Informed Consent of all Living Donors (Living Donor Committee) 8
12. Proposal for the Definition of Pancreas Graft Failure (Pancreas Transplantation Committee) 8

Other Committee Work **9**

Meeting Summaries **9**

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This report reflects the work of the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee during the June 2014 to September 2014 period.

Action Items

1. Proposal to Cap the HCC Exception Score at 34

Public Comment: March 14, 2014- June 13, 2014

Candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list, especially as their exception scores may increase automatically every three months. Increasingly, there are candidates with multiple HCC exception extensions who are now receiving regional offers under the "Share 35 Regional" policy implemented in June 2013. However, candidates with HCC exceptions are likely to have a much lower risk of disease progression or dropout (i.e., removal from the waiting list for death or being too sick) than those without HCC exceptions. This proposal will cap the HCC exception score at 34, in effect giving candidates with calculated MELD/PELD scores of 35 and higher a better opportunity to receive regional offers under the new policy.

The Committee considered and addressed public comment feedback on its proposed language. After careful consideration, the Committee unanimously voted in support of forwarding the proposal to the Board for consideration by a vote of 15 in favor, 0 opposed, and 0 abstentions during an in-person meeting on September 17, 2014.

RESOLVED, that the additions and modifications to Policy 9.3.G.vi (Extensions of HCC Exceptions), as set forth in Exhibit A, are hereby approved, effective pending programming and notice to the OPTN membership.

2. Proposal to Delay the HCC Exception Score Assignment

Public Comment: March 14, 2014- June 13, 2014

Candidates with a MELD/PELD score exception for HCC receive high priority on the liver waiting list, especially as their exception scores may increase automatically every three months. These candidates have significantly lower dropout rates (i.e., removal from the waiting list for death or being too sick) than non-HCC candidates, with the exception of those areas of the country with lengthy waiting times. The proposed solution to address the disparities in drop-out rates between patients with HCC exceptions and those without is to delay the score assignment by 6-months. Simulation modeling has shown that this would reduce the disparity in the transplant and drop-out rates for those with and without HCC exceptions. In areas of the country with shorter waiting times to transplant, the delay will also allow a window of time for centers to observe candidates with rapidly growing tumors who may have very poor outcomes with a transplant.

The Committee considered and addressed public comment feedback on its proposed language. After careful consideration, the Committee voted in support of forwarding the proposal to the Board for consideration by a vote of 14 in favor, 0 opposed, and 1 abstentions during an in person meeting on September 17, 2014.

RESOLVED, that the additions and modifications to Policy 9.3 G (Candidates with Hepatocellular Carcinoma), as set forth in Exhibit B, are hereby approved, effective pending programming and notice to the OPTN membership.

Committee Projects

3. Liver Distribution Redesign Modeling (Redistricting of Regions)

Public Comment: To be determined
Board Consideration: To be determined

Despite continued improvements in liver allocation and distribution over the last 15 years, waitlist mortality remains high for candidates with higher MELD/PELD scores. Significant disparity exists between OPOs and regions with regard to the mean MELD/PELD score at transplant and waitlist mortality. The Committee has been examining ways to direct livers to those most in need. The concept of redistricting, similar to the methodology used in designing school and political districts, was introduced to the Committee. Simulation modeling suggests that optimized or fewer geographic districts would likely reduce the variation in MELD/PELD score at transplant and reduce waitlist deaths.

In April 2014, the Committee endorsed the redistricting concepts and agreed to 1) educate the community about the concepts and 2) solicit feedback from the broader community before releasing a public comment proposal on the topic. In June, the Committee therefore released a concept document along with a questionnaire seeking community input on the concept. A total of 692 responses, as well as 6 letters, were received in response. These responses were analyzed to form the basis of an agenda and to identify potential key speakers for a public forum on Redesigning Liver Distribution, held in Chicago on September 16, 2014.

A total of 264 people were in attendance at the Forum, and an additional 282 participated on-line via Go-To-Webinar®. The purpose of the forum was to further the conversation about various concepts intended to increase equity in access to liver transplantation, as well as special considerations related to broader sharing, such as cost, clinical impacts, logistical and collaborative efforts. Presenters and participants from across the country contributed to the success of the forum.

The forum was successful in its intended purpose, which was to gather additional feedback, ideas and questions to help shape further policy development. The vast majority of participants agreed that the OPTN should seek to ensure that candidates have timely access to liver transplantation. Opinions varied about the best metrics and methods to use for reducing geographic disparities, as well as the potential effects that redistricting may have for transplant centers in terms of clinical practice, logistics and costs. The importance of optimizing organ donation and the utilization of available organs was also discussed at length.

The Liver and Intestinal Organ Transplantation Committee met on September 17, 2014 to discuss the feedback from the forum. The Committee agreed that additional study and

feedback is necessary in several areas prior to any policy development. The Committee established several working groups, each composed partly of members of the committee and partly of additional subject matter experts. These working groups will address three key focus areas: metrics to assess geographic disparity, logistical/transportation considerations, and financial issues.

The work groups will develop recommendations to be shared with the full committee by the spring of 2015 to aid in refinement of existing concepts or development of new ones. Additionally, the Liver Utilization subcommittee will be reconvened to address issues related to decreasing liver discards in order to increase the number of livers available for transplantation.

Although the Committee does not intend to abandon the concept of Redistricting entirely, they will revisit the metrics of disparity and optimization of maps. Additionally the Committee plans to reconsider the benefits of eight to eleven optimized districts previously presented by the SRTR and new concepts such as Districts that utilize concentric circles as a local tier.

4. National Review Board for MELD/PELD Exceptions

Public Comment: January, 2015 (*Estimated*)
Board Consideration: June, 2015 (*Estimated*)

In November 2013, the Board of Directors directed the Committee to develop a plan for a National Review Board (NRB) for MELD/PELD exceptions. At the June 2014 Board meeting, the Committee presented the preliminary construct for an NRB, and requested Board feedback. The Board was supportive of the concept and urged the Committee to continue the work. The goal of an NRB is to promote consistent reviews across the country.

The construct that the Committee presented to the Board is similar to one that was circulated for public comment in 2004. Each region would select 10 experienced representatives who would serve a 2-3 year term with a two term limit. Cases submitted for review would be assigned randomly to 7 members of the review board and would be closed when 4 members have voted; much like the way the current RRB process functions. Pediatric cases would be reviewed by pediatric providers and adult cases would be reviewed by adult providers. Additional standardized guidelines for approving MELD/PELD exception cases will be developed, to be used by the NRB to promote consistent reviews.

A proposal will likely be circulated in the spring of 2015 for community consideration.

5. Develop materials to Educate RRB Members and Promote Consistent

Public Comment: To be determined
Board Consideration: To be determined

Regional Review Board members have varying degrees of understanding about their duties, liver allocation policies, and the RRB process. The Committee has reviewed the prior and current RRB Operational Guidelines. Committee members have identified differences in the way RRBs operate (e.g., some have regular calls, some meet at Regional meetings; some have specific criteria for exceptions or timeframes for voting, etc.). The Committee has also identified the need to better educate incoming and new RRB members about MELD/PELD exception policies.

At the request of the Committee and in conjunction with the liver transplant programs in Region 5, staff have developed educational materials currently being piloted with the newest incoming RRB members in Region 5. This online tutorial includes a slide set with speaker notes and an assessment tool. Additionally, rotation schedules were updated to eliminate many of the complications attributed to constant member turnover. The first group to pilot this effort completed the tutorial provided. In December, half of this group will rotate off the current Board and new members will be provided the same online tutorial.

While it is too early to determine if these materials have impacted the process of the RRB, the Committee will continue to monitor the effort and plan to expand nationally if the pilot is shown to improve the system.

6. Proposed Membership and Personnel Requirements for Intestine Transplant Programs

Public Comment:	March 14, 2014 - June 13, 2014
	January, 2015 (*Estimated*)
Board Consideration:	June, 2015 (*Estimated*)

There are currently no OPTN/UNOS requirements for qualifying intestinal programs, physicians, and surgeons. Currently, any transplant program that is approved to perform liver transplants can perform intestinal transplants. The Committee submitted a proposal for Membership and Personnel Requirements for Intestine Transplant Programs for public comment in August 2006, but it was not well supported, and the proposal was withdrawn. The main concerns expressed were that a large number of well-qualified programs and smaller volume programs would not be able to meet these requirements and that that no training program in the country would have met the requirements as written. The proposal also did not contain a transition plan for existing programs. The LTC was aware that the American Society of Transplant Surgeons (ASTS) was developing its own criteria for intestinal program accreditation that would set levels for volume and experience, so it agreed to postpone this effort until after the ASTS made its recommendations.

The ASTS finalized its criteria for fellowship training programs in September 2008. A Subcommittee of the LTC made initial recommendations applying the bylaws for liver transplant surgeons and physicians with the ASTS volume numbers (10 transplants per year) as a starting point. These were presented to the MPSC in November 2009, and objections were expressed similar to ones regarding the prior proposal. In December 2012, the Subcommittee presented recommendations to the MPSC, and once again, concerns about the volume requirements were expressed because the number of intestine transplant surgeries has been declining since 2007. Concerns about how the bylaw would be implemented also resurfaced. In order to facilitate better cross-committee communication, a joint Liver-MPSC subcommittee was created in the fall of 2013. This joint subcommittee made several modifications to the proposal to address the concerns that had been expressed.

The Proposal for Membership and Personnel Requirements for Intestine Transplant Programs was circulated for public comment from March 14, 2014 - June 13, 2014. 17 responses, in addition to the regional and Committee responses were received. While public comment was largely favorable, with 90% in favor, only 1 region, and 1 committee voting in opposition, commenters called for additional amendments to the proposal including the need

for a designated dietician, affiliation with a gut rehabilitation program and a less constraining time limit on the requirements for full approval. Additionally a more detailed plan for transition of existing programs was requested.

The Committee recognized an opportunity to further improve the proposal before presenting it to the Board for consideration. The proposal is being redrafted to address the concerns of the community and will be recirculated for public comment in the spring of 2015.

7. Ongoing Review of MELD/PELD Exceptions

Public Comment: N/A
Board Consideration: June, 2015 (*Estimated*)

The MELD Exceptions and Enhancements Subcommittee has been reviewing the types of MELD exceptions submitted to the Regional Review Boards (RRBs), with the intent of providing an update to the MELD Exceptional Study Group (MESSAGE) exception guidelines published in 2006. The Subcommittee reviewed all of the non-HCC initial MELD exception requests submitted between May 1, 2012 and April 30, 2013. While thirty percent fell into categories that are included in the current policies (e.g., cholangiocarcinoma, familial amyloidosis, etc.) several other diagnoses accounted for a large proportion of the non-standard diagnoses: neuroendocrine tumors (NET), polycystic liver disease (PCLD) and primary sclerosing cholangitis (PSC).

Subcommittee members reviewed the literature for NET, PCLD and PSC and drafted exception guidelines for those diagnoses. The Subcommittee also reviewed the literature for the diagnoses currently included in the policies, and agreed that those policies should not be changed at this time. "Guidance to Liver Transplant Programs and Regional Review Boards for MELD/PELD Exceptions submitted for Neuroendocrine Tumors and Polycystic Liver Diseases," was approved by the Board at the Board 2014 meeting and became effective June 24, 2014.
The guidance document includes the criteria for exceptions that should be considered by the RRBs for these diagnoses, but does not include recommendations for point assignments, as these would likely vary by region. These will be used as guidelines until enough experience and evidence is gained to formulate policy. The Committee is still developing guidelines for PSC, which will be submitted to the Board in June 2015.

Committee Projects Pending Implementation

8. Adding Serum Sodium to the MELD Score

Public Comment: March 15, 2013- June 15, 2013
Board Approval: June, 2014
Implementation Date: To be determined

The Board approved the proposal to incorporate serum sodium into the MELD score calculation in June 2014. This included a Board amendment that would restrict the additional points for sodium to only those candidates with a MELD score (as currently calculated) of 12 or higher. Data from the University of Michigan showed that patients with a MELD score below 12 would not benefit from adding serum sodium points to their MELD score calculation. These data suggest that the incorporation of serum sodium may lead to an increased chance of transplantation in candidates who may not benefit from transplantation at that time.

This policy is pending programming and will become effective upon implementation. Once programmed, the system will automatically calculate candidates' new MELD score. The Committee has requested a 7-day "grace period" during implementation for those candidates whose scores would be moved from one recertification category to another, and may as a result require immediate recertification (i.e., the candidates would face an immediate "downgrade" of their MELD score). If a center has not recertified these candidates on the 8th day after implementation, the candidates will be downgraded to their previous lower MELD score as is done currently when certification expires.

9. Re-instate the No Appeal, No Withdrawal Button for Denied MELD/PELD Exceptions

Board Approval: June, 2009
Implementation Date: Second half of 2015

Policy 3.6.4.5 states that "Each RRB must set an acceptable time for reviews to be completed, within twenty-one days after application; if approval is not given within twenty-one days, the patient's transplant physician may list the patient at the higher MELD or PELD score, subject to automatic referral to the Liver and Intestinal Organ Transplantation and Membership and Professional Standards Committees." When this policy was approved in November 2001, the 21-day time frame was intended to provide adequate time for dialogue between the physician and the RRB, while allowing the treating physician to make the ultimate decision regarding the candidate's listing, with the knowledge that the case would be referred to the Liver Committee and potentially the MPSC. When first implemented, the listing center could select the "no appeal/no withdraw" ("override") button on the application after a denial by the RRB. If this button was selected, the candidate would be assigned the requested score, with a warning that the case would be referred to the Liver Committee and potentially the MPSC. The button was last utilized by a center in 2003, and was inadvertently removed when a modification to the policy was subsequently implemented. Listing physicians still have the option of last-minute appeal of denied cases, but the Committee did not feel that is an appropriate solution. The Committee recommended that the "no appeal/no withdraw" should button be reinstated.

In June 2009, the Board approved a proposal to reinstate the MELD/PELD exception "override" button. This would enable a treating physician to make the ultimate decision regarding the candidate's listing in cases when the physician and the Regional Review Board (RRB) cannot reach an agreement. Such cases would be referred to the Liver Committee for additional review. This project is awaiting implementation.

Implemented Committee Projects

10. Proposal for Regional Distribution of Livers for Critically Ill Candidates, (Share 35)

Public Comment: September 16, 2011- January 12, 2012
Board Approval: June, 2012
Implementation Date: June 18, 2013

The "Share 35" liver allocation policy was implemented on June 18, 2013. The policy gives greater priority to candidates with MELD/PELD scores of 35 and higher. The Committee has been monitoring the impact of the policy to ensure that the results are as intended. The one-year data analyses were presented on September 4, 2014 **(Exhibit C)**. As expected, the percentage of regional sharing increased, from 20.4% to 33.3% of deceased donor

transplants. The percentage of transplants in recipients with MELD/PELD scores of 35 and higher increased from 18.7% to 26.3%. Overall waiting list mortality was unchanged, at 18.5%. The number of livers discarded decreased nationally. In Regions 1, 4, 8 and 10, where discards increased, the number of transplants also increased. Six-moth post-transplant patient survival rates were unchanged pre- and post-Share 35. The Committee will continue to review the effects of Share 35 at six-moth intervals.

The logistical issues related to broader sharing and reports of unprofessional behavior during the first few months post implementation seem to have subsided. However, the Committee will continue to explore standards and guidelines that will increase efficiency and strengthen professional relationships in facilitating broader sharing.

Review of Public Comment Proposals

The Committee reviewed 3 of the 17 policy proposals released for public comment from March – June, 2014. The review of 2 of these 3 proposals were reported in the June 2014 Board Report, the third is provided below. Additionally, the Committee has reviewed 1 of the 18 proposals currently in Public Comment.

11. Proposal to Modify Existing or Establishing New Requirements for the Informed Consent of all Living Donors (Living Donor Committee)

The Committee considered this proposal in November 2013 prior to the formal release for public comment. The intent of this policy is to standardize the informed consent of living kidney donors, which has already been established. Additionally, this proposal would modify some elements of exiting policy for the informed consent of living kidney donors and establish new requirements for all other categories of living organ donors.

While the number of living lung, pancreas and intestine donors is very low, these donors are not addressed under any existing OPTN policy or bylaws for living donor consent or medical evaluation. As currently proposed, the OPTN would have general consent and medical evaluation policies that would apply to all types of living donors, and other consent and medical evaluation policies that would be specific to living kidney and liver donors. The Committee felt that it makes sense to apply these protections to all types of living donors and therefore supports this proposal although no formal vote was taken.

12. Proposal for the Definition of Pancreas Graft Failure (Pancreas Transplantation Committee)

The Committee reviewed the Pancreas Transplantation Committee's proposal released for public comment from September 29, 2013- December 12, 2014. Currently there is no nationally and consistently used definition for identifying and documenting pancreas graft failure. This has led to variation in how transplant programs report pancreas graft failure to the OPTN/UNOS and, consequently, limits the Membership and Professional Standards Committee's (MPSC) ability to consistently analyze and compare pancreas program outcomes. The Pancreas Transplantation Committee has developed a proposal to define when graft failure occurs, which will subsequently lead to consistent reporting. Additionally, Tiedi Help Documentation will be added explaining how to document pancreas graft failure, and updates to the Teidi forms will be made.

The proposed changes define pancreas graft failure when any of the following occurs:

- A recipient's transplanted pancreas is removed
- A recipient re-registers for a pancreas
- A recipient registers for an islet transplant after receiving a pancreas transplant
- A recipient's insulin use is greater than or equal to 0.5 units/kg/day for a consecutive 90 days
- A recipient dies

Some members of the Committee inquired how the Pancreas Transplantation Committee had determined the level of insulin use as 0.5 units/kg/day for failure and suggested perhaps that any patient requiring insulin more than 90 days post-transplant should be considered a graft failure. Another Committee member suggested incorporating C-peptide into the algorithm, for failure, especially in consideration of the insulin resistant population, which is increasing due to the obesity epidemic. The Pancreas Committee representative stated that this proposal contained minimum criteria and that there may be room to expand at a later date. Committee members acknowledged that the Pancreas Committee had kept the best interest of the patients in mind with this proposal and although no vote was taken, the Committee was generally supportive.

The Pancreas Transplantation Committee also requested that the Committee consider whether the current general definition of "Graft Failure," in Policy 1.2 Definitions, applies across all organ types, or if there should be organ-specific definitions of graft failure. Committee members agreed that the current definition in Policy 1.2 (Definitions) is antiquated and that organ-specific definitions should be developed and anticipate developing recommendations for the definition of liver graft failure if a formal project is pursued and approved.

Other Committee Work

None

Meeting Summaries

The committee held meetings on the following dates:

- June 3, 2014
- August 6, 2014
- September 4, 2014
- September 17, 2014

Meetings summaries for this Committee are available on the OPTN website at:
http://optn.transplant.hrsa.gov/converge/members/committeesDetail.asp?ID=25.